isopropyl *p*-toluenesulfonate (177 g, 0.8 mol) and sodium cyanide (53 g, 1.08 mol) in DMSO (250 ml) according to the procedure[40] used to convert alkyl halides into nitriles. The yield of heptadeuterioisobutyronitrile, bp 103–105°, n^{24}D 1.3706 (lit.[41] bp of d_0 compound 103.5°, n^{15}D 1.37563), was 28%.

2-Methyl-d_3-propyl-2,3,3,3-d_4-amine. Reduction[32] of heptadeuterioisobutyronitrile (7.5 g, 0.1 mol) with lithium aluminum hydride (7.6 g, 0.2 mol) yielded 81% of 2-methyl-d_3-propyl-2,3,3,3-d_4-amine (6.4 g, 0.08 mol), bp 67–69°, n^{22}D 1.3963 (lit.[37] bp of d_0 compound 69°). The deuterium content of the amine was 7% d_6 and 94% d_7 as determined by low-voltage mass spectrometry. Nmr showed that most of the d_6 was a result of hydrogen on a methyl group.

Ethyl Methylmalonate. Decarbonylation of ethoxalyl propionate gave ethyl methylmalonate.[42] The yield of distilled material, bp 195–196°, n^{28}D 1.4092 (lit.[42,43] bp 194–196°, $n^{16.8}$D 1.4148), was 89%.

2-Methyl-4,4,4-d_3-butyric Acid. Alkylation of ethyl methylmalonate (174 g, 1 mol) with ethyl-2,2,2-d_3 *p*-toluenesulfonate (152.5 g, 0.75 mol), followed by ester hydrolysis and decarboxylation, according to the procedure used to prepare pelargonic acid,[44] gave 2-methyl-4,4,4-d_3-butyric acid (31.5 g, 0.31 mol), bp 173–177° (lit.[45] bp of d_0 compound 177°), in a 41% yield. The infrared spectrum was identical with that of known 2-methylbutyric acid except for a sharp absorption at 4.51 μ which is attributable to carbon–deuterium stretching vibrations.

***sec*-Butyl-4,4,4-d_3-amine.** Chilled concentrated sulfuric acid[46] (250 ml) was added dropwise at 0° to 2-methyl-4,4,4-d_3-butyric acid (31.5 g, 0.31 mol). The mixture was heated to 40° and sodium azide (22.8 g, 0.35 mol) was added at such a rate that the temperature in the reaction flask did not go above 50°. Upon the completion of the addition of sodium azide, the mixture was heated at 120° for 12 hr.[47] The solution was neutralized with concentrated potassium hydroxide and then extracted with three 100-ml portions of ether. The ether extract was dried over sodium sulfate and HCl gas was bubbled into the ether solution. A tan solid precipitated. The solid was dissolved in water and treated with charcoal. The water was stripped off leaving white *sec*-butyl-4,4,4-d_3 amine hydrochloride (24.4 g, 0.22 mol, 70%), mp 144–146° (mp of d_0 compound 147–148°). A weak nmr signal was observed for the C-4 methyl hydrogens and low-voltage mass spectrometry showed the deuterium content to be 4.4% d_2 and 95.6% d_3.

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[40] L. Friedman and H. Shechter, *J. Org. Chem.*, **25**, 877 (1960).

[41] *Cf.* ref 37, Vol. V, p 1902.

[42] R. F. B. Cox and S. M. McElvain, "Organic Syntheses," Coll. Vol. II, John Wiley & Sons, Inc., New York, N. Y., 1943, p 279.

[43] G. Wittig, M. Heintzeler, and M. H. Wetterling, *Ann.*, **557**, 204 (1947).

[44] E. Reid and J. R. Ruhoff, "Organic Syntheses," Coll. Vol. II, John Wiley & Sons, Inc., New York, N. Y., 1943, p 474.

[45] *Cf.* ref 37, Vol. IV, p 2150.

[46] T. Moritsugu, Ph.D. Thesis, Ohio State University, Columbus, Ohio, 1954.

[47] It was subsequently found that heating for 1 hr at 100° was adequate.

Alkylation of Arenes *via* Aprotic Diazotization of Alkylamines[1]

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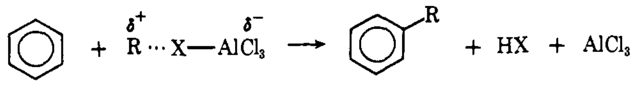
Abstract: Alkylation of arenes *via* aprotic diazotization of aliphatic amines gave low yields of substituted arenes. Its value as a preparative method is negated by the low yields (0.5–2.5%); however, the reaction was studied because of its theoretical interest. The minor amounts of rearrangement that occured in the alkylarene fraction suggests that the intermediate involved is short lived, and that π-complex formation predominates. The isomer composition of cymenes from diazotization of isopropylamine in toluene and the relative selectivity exhibited by isopropylation in toluene–benzene mixtures suggest that cationic intermediates are involved in aprotic diazotizations.

Cationic intermediates from various precursors have been shown to be involved in Friedel–Crafts alkylation. Formation of a carbonium ion was originally postulated;[3] however, subsequent studies[4] indicated that a displacement by the aromatic ring on the alkyl derivative–catalyst complex was also involved. Kinetic studies on methylation,[4c] ethylation,[4c] and benzylation[4a] with alkyl chlorides and aluminum chloride showed a first-order dependence on arene. Thus the displacement by the arene on the alkyl derivative–catalyst complex was postulated to be the rate-controlling step in the reaction. In cases where stabilization might occur (*i.e.*, *t*-butyl cation) a carbonium ion could be involved; however, it has been suggested[5] that even this is at best an ion pair rather than a free carbonium ion.



The exact mechanistic features of Friedel–Crafts reactions are dependent on the solvent system and the electrophile involved.[6] Either σ-complex[4a–d] or π-

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[1] (a) Financial support (Grant No. GP-3976) from the National Science Foundation in gratefully acknowledged. (b) A preliminary account of a portion of this work has been published: A. T. Jurewicz, J. H. Bayless, and L. Friedman, *J. Am. Chem. Soc.*, **87**, 5788 (1965). (c) For the preceding paper in this series, see L. Friedman and A. T. Jurewicz, *ibid.*, **91**, 1803 (1969).

[2] Based on the Ph.D. dissertation of A. T. Jurewicz, Case Institute of Technology, 1967.

[3] C. C. Price, *Org. Reactions*, **3**, 1 (1946); C. C. Price, *Chem. Rev.*, 29, 37 (1941).

[4] (a) H. C. Brown and M. Grayson, *J. Am. Chem. Soc.*, **75**, 6285 (1953); (b) H. C. Brown and H. Jungk, *ibid.*, **77**, 5584 (1955); (c) H. Jungk, C. R. Smoot, and H. C. Brown, *ibid.*, **78**, 2185 (1956); (d) C. R. Smoot and H. C. Brown, *ibid.*, **78**, 6249 (1956); (e) G. A. Olah, S. J. Kuhn, and S. H. Flood, *ibid.*, **84**, 1688 (1962).

[5] G. A. Olah, S. H. Flood, and M. E. Moffatt, *ibid.*, **86**, 1060 (1964).

[6] G. A. Olah, S. H. Flood, S. J. Kohn, M. E. Moffatt, and N. A. Overchuck, *ibid.*, **86**, 1046 (1964).

complex[4–6] formation has been postulated to be the rate-determining step. Since in either mechanism, intermediates of cationic character are involved, a study of possible electrophilic aromatic substitution from intermediates of amine diazotizations was undertaken. We now would like to report on this study.

Results and Discussion

Diazotization of alkylamines in benzene with decyl nitrite[7] gave alkylarenes in low yields (Table I). The total amount of substitution ranged from 0.2% with isobutylamine to 2.5% with *n*-butylamine. Highest yields were obtained with primary straight-chain amines, and this is in accord with the ease of direct SN2 displacement on a diazonium ion–gegenion pair.[8] Thus the reaction is unimportant preparatively,[9] but is of theoretical interest, since it was previously suggested that aprotic deaminations involved intermediates of cationic character.[10]

Minimal rearrangement of the alkyl group occurred; *e.g.*, deamination of *n*-butylamine in benzene gave an arene fraction which consisted of 98% *n*-butylbenzene and 2% *sec*-butylbenzene. Similar results were obtained with *n*-propylamine.[11] These results are in direct contrast with those obtained from the reaction of alkyl chlorides with aluminum chloride. In these cases extensive rearrangement occurred, *e.g.*, *n*-butyl chloride with aluminum chloride at 0° for 2.5 hr gave 64% *sec*-butylbenzene and 36% *n*-butylbenzene.[12] When the alkylation is carried out at higher temperatures, 80°, isobutylbenzene is formed,[12] thus indicating that subsequent rearrangements occurred.[11]

Deamination of isobutylamine gave an alkylarene fraction containing 7% *sec*-butylbenzene and 93% isobutylbenzene. No *t*-butylbenzene was detected. Similarly, *t*-butylbenzene was not formed from diazotization of *t*-butylamine;[13] the major product was isobutylene. In general, formation of *t*-butyl derivatives in aprotic deamination rarely occurs; *e.g.*, isobutylamine gave a substitution fraction containing 5% *t*-butyl, 9% *sec*-butyl, and 86% isobutyl derivatives.[14] Since isobutylene formation occurs predominantly from *t*-butyl precursors in aprotic media,[13] it is not surprising that the weakly nucleophilic arenes do not trap it. In Friedel–Crafts alkylations, isobutyl chloride gave only *t*-butylbenzene;[12,15] however, in these systems the *t*-butyl cation is stabilized by AlCl$_4^-$.

Table I. Alkylation of Benzene[a]

	Alkylarenes		
	% yield[b,c]		Product
Amine	HOAc[d]	HCl[d]	composition[e]
n-Propyl	0.65	1.6	97% *n*-propyl, 3% isopropyl
n-Propyl[f]	0.4		92% *n*-propyl, 8% isopropyl
Isopropyl	0.5	1.1	100% isopropyl
n-Butyl	1.5	2.5	98% *n*-butyl, 2% *sec*-butyl
Isobutyl[g]	0.2	0.4	93% isobutyl, 7% *sec*-butyl
sec-Butyl	0.3	0.5	100% *sec*-butyl

[a] Amine (10 mmol), acid (10 mmol), and decyl nitrite (11 mmol) in 100 ml of benzene at reflux. [b] Quantitative glpc. [c] Average of several runs. [d] Total yields of alkylarenes when HOAc and HCl are proton sources, respectively. [e] Independent of proton source. [f] *Cf.* ref 20. [g] Nmr analysis of poorly resolved glpc collected products indicated 6–10% *sec*-butylbenzene.

Table II. Decomposition of N-Nitroso-N-alkylacetamides in Benzene[a]

	Alkylarenes	
N-Nitroso-N-alkylacetamide	% yield[b,c]	Product composition
n-Butyl	1.5	98.7% *n*-butyl, 1.3% *sec*-butyl
Isopropyl	0.8	100% isopropyl

[a] N-Nitroso-N-alkylacetamide in refluxing benzene. [b] Quantitative glpc. [c] Average of several runs.

In all the systems studied, where rearrangement was possible, only minor amounts were observed. This suggests that direct displacement by the arene on a diazonium ion–gegenion pair occurs; however, the exact mode of attack is unknown since in the rate-determining step either π- or σ-complex formation is possible. π-Complex formation is thought to be irreversible (when the reaction is effected in nitromethane) and to have a transition state that resembles reactants.[4e,5,6] This is in accord with the observed results since little rearrangement occurs and suggests that π-complex formation is occuring.

The minor amounts of rearrangement can be attributed to either rearrangement in the π complex[16] or loss of nitrogen from diazonium ion to give a rearranged carbonium ion,[17] which is then trapped by the arene.

Alkylation of benzene also occurred when N-nitroso-N-alkylacetamides were thermally decomposed in benzene (Table II). Essentially identical results were

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(7) Identical results were obtained with amyl nitrite; however, glpc analytical problems were avoided when decyl nitrite was used.

(8) Diazonium ion–gegenion pairs have been suggested as the primary reactive intermediates: J. H. Bayless, A. T. Jurewicz, and L. Friedman, *J. Am. Chem. Soc.*, **90**, 4466 (1968). This is an extension of the previously described diazonium ion theory in the effect of the gegenion is considered: A. Streitwieser, Jr., *J. Org. Chem.*, 22, 861 (1957); *cf.* E. H. White and C. A. Aufdermarsh, Jr., *J. Am. Chem. Soc.*, **83**, 1179 (1961); T. Cohen and F. Jankowski, *ibid.*, **86**, 4217 (1964); E. H. White and F. W. Bachelor, *Tetrahedron Lett.*, 77 (1965).

(9) It has recently been shown that better yields (25–50%) of alkylarenes can be obtained by the reaction of alkylsulfinylamines and isocyanates with nitrosonium salts; *e.g.*, NO$^+$PF$_6^-$, NO$^+$BF$_4^-$, and NO$^+$SbF$_6^-$: G. A. Olah and E. Namanworth, *J. Am. Chem. Soc.*, **88**, 5328 (1966). The higher yields reported here are probably due to the fact that the gegenion is a weak nucleophile and that no water is produced in the nitrosation process; *i.e.*, Friedel–Crafts reaction conditions are approached.

(10) A. T. Jurewicz and L. Friedman, *ibid.*, **89**, 149 (1967).

(11) There is no effect of temperature on the extent of rearrangement. When the reaction was carried out at 30° *n*-propylamine gave 3% isopropylbenzene and 97% *n*-propylbenzene.

(12) R. M. Roberts and S. Shiengthong, *J. Am. Chem. Soc.*, 82, 632 (1960).

(13) Deaminations in ethers (glyme and *n*-butyl ether) gave products resulting form ether cleavage. However, no *t*-butyl products were observed from either isobutylamine or *t*-butylamine deaminations: L. Friedman and J. H. Bayless, submitted for publication.

(14) J. H. Bayless, F. D. Mendicino, and L. Friedman, *J. Am. Chem. Soc.*, 87, 5790 (1965).

(15) (a) J. Schramm, *Monatsh. Chem.*, **9**, 613 (1888); (b) M. Senkowski, *Chem. Ber.*, 23, 2412 (1880); (c) M. I. Konowalow, *J. Russ. Phys. Chem.*, 27, 456 (1895); *Bull. Soc. Chim. Fr.*, **16**, 864 (1896).

(16) No reaction occurred between 2-pentanol and boron trifluoride in pentane, but a polymer was obtained when the reaction was carried out in hexaethylbenzene. It was suggested that a π complex of the 2-pentyl cation occurred in the arene and subsequently reacted to form polymer: A. Streitwieser, Jr., W. D. Schaeffer, and S. Andreades, *J. Am. Chem. Soc.*, **81**, 1113 (1959).

(17) It has also been suggested that the only carbonium ions formed in aprotic diazotizations are those formed *via* rearrangement.[8]

Table III. Diazotization of Alkylamines in Benzene[a]

Reactants	Composition[c]	
	Alkylarenes[b]	Acetate derivatives
n-Propylamine–HOAc–RONO	97% *n*-propyl, 3% isopropyl	97% *n*-propyl, 3% isopropyl
n-Propylamine–HOAc–RONO[d]	92% *n*-propyl, 8% isopropyl	92% *n*-propyl, 8% isopropyl
n-Butylamine-HOAc–RONO	98% *n*-butyl, 2% *sec*-butyl	98% *n*-butyl, 2% *sec*-butyl

[a] Amine (1 equiv), HOAc (1 equiv), and decyl nitrite in 100 ml of refluxing benzene. [b] From Table I. [c] Glpc analyzed. [d] Reaction conditions employed in ref 20.

Table IV. Isopropylation of Benzene–Toluene Mixtures[a]

Reactants	Cymene isomer content[b]			Toluene:benzene volume ratio	Obsd rel rates	Rel rates according to first-order dependence in aromatics
	ortho	*meta*	*para*			
Isopropylamine–HOAc–RONO[c]	40	26	34	1:1	1.52	1.52
	41	24	35	1:3	0.68	2.04
	39	26	35	3:1	4.92	1.64
d	42	24	34	1:1	2.86	2.86
Isopropylamine–HCl–RONO[c]	40	27	33	1:1	1.76	1.76
	40	26	34	1:3	0.62	1.86
	39	27	34	3:1	5.37	1.79
N-Nitroso-N-isopropylacetamide[e]	39	25	36	1:1	1.72	1.72
	41	24	35	1:3	0.60	1.80
	40	26	34	3:1	5.28	1.76

[a] Reactants (50 mmol) in 100-ml of toluene–benzene mixture. [b] Glpc analyzed. [c] Heterogeneous. [d] Reaction conditions according to ref 20 except that decyl nitrite was used; single run. [e] Homogeneous.

obtained from N-nitroso-N-*n*-butylacetamide and *n*-butylamine. This supports the concept that common intermediates are involved when the two reactions are effected in nonpolar solvents.[18]

The extent of rearrangement in the alkylarene fraction is identical with that in the counterion products (Table III). These results indicate that the minor amounts of rearrangement observed in the alkylarene fraction occurred prior to the attack by the arene.[19] The results in the alkylarene and acetate fractions also imply that the partitioning of the diazonium ion and the rearranged carbonium ion is the same for the alkylarenes and acetates. Thus the ratio of nucleophilicities of acetate anion and arene appears to be the same for attack on diazonium ion or carbonium ion.

A report of aromatic alkylation *via* diazotization was published[20] while this investigation was in progress. Several major differences were reported: (1) *n*-propylamine gave an arene fraction containing 55% isopropylbenzene and 45% *n*-propylbenzene, (2) somewhat higher yields (3–4%) of cumene were obtained, and (3) isopropyl acetate was a major product. Reinvestigation of the alkylation *under the conditions described*,[20] except that glpc analysis was made directly on the reaction mixture rather than after sulfuric acid treatment,[21] resulted in a isomer composition of 8% isopropylbenzene and 92% *n*-propylbenzene. Identical isomer composition was observed in the acetate fraction. Under these conditions[20,22] the molar ratio of solvent to labile protons[23] is between 1.45 and 2.9, whereas the ratio is between 10 and 20 under the aprotic conditions used in this study. Thus increased stabilization would be expected in the former, and therefore increased rearrangement (8 *vs.* 3%) is further indication of the importance of the *total* solvent system.

In order to determine the relative selectivity of the species toward benzene and toluene, isopropylation was studied since the analytical problems are minimized in that only cumene and cymenes are formed (Table IV).

Competition experiments are valid only if the relative rates are dependent on the aromatic substrate. In order to substantiate this, and to determine whether the counterion is a factor, experiments were carried out in various toluene–benzene mixtures. A k_T/k_B of 1.81 ± 0.23 with acetic acid and 1.72 ± 0.14 with hydrochloric acid was obtained. These values are essentially identical when the deviation is considered and thus selectivity is not acid dependent. However, since the reactions are not completely homogeneous (water is formed), especially with the amine hydrochloride, experiments using N-nitroso-N-isopropylacetamide were made. A k_T/k_B of 1.76 ± 0.04 was obtained.[24] These values are similar to ratios obtained for Friedel–Crafts isopropylations in nitromethane.[6]

The cymene isomer composition, 40–42% *ortho*, 22–24% *meta*, and 33–35% *para*,[25] was independent of the mode of diazonium ion generation. The *meta* value is higher than the 14–19% obtained in Friedel–

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[18] J. H. Bayless and L. Friedman, *J. Am.Chem. Soc.*, **89**, 147 (1967).

[19] It is possible that rearrangement occurred in the π complex and then gave both rearranged acetates and alkylarenes. However, similar amounts of rearrangement in the acetate fraction is obtained in nonaromatic solvent.[14]

[20] D. E. Pearson, C. V. Breder, and J. C. Craig, *J. Am. Chem. Soc.*, **86**, 5054 (1964).

[21] Cumene is formed from isopropyl alcohol, benzene, and sulfuric acid. No alkylation with *n*-propyl alcohol was observed.

[22] Amine (0.02 mol), HOAc (0.02 mol), and butyl nitrite (0.02 mol) in 6 ml of arene are the conditions that were employed.

[23] For every equiv of nitrite used, 1 equiv of alcohol and water is formed. Originally 1 equiv of acetic acid is present but is partially consumed in ester formation. These proton sources are in effect solvating agents.

[24] The smaller deviation obtained with N-nitroso-N-isopropylacetamide suggests that part of the difficulties encountered in amine deaminations was partially due to formation of water and resulting heterogenous reaction conditions.

[25] We acknowledge with thanks Professor G. A. Olah for authentic samples of *o*-, *m*-, and *p*-cymenes.

Table V. Isopropylation of Anisole[a]

	Isopropylanisole isomer distribution[b]		
Acid	*ortho*	*meta*	*para*
HOAc	58	5.5	36.5
HCl	58	5	37

[a] Isopropylamine (10 mmol), acid (10 mmol), and decyl nitrite (11 mmol) in 100 ml of anisole at 100°. [b] Duplicate runs.

Crafts isopropylation in nitromethane,[6,26] where isomerization of the initially formed isomers is minimal.

Isopropylation of anisole *via* aprotic diazotization gave a mixture of 58% *o*-, 5% *m*-, and 37% *o*-isopropylanisoles, *ortho/para* = 1.6 (Table V).[27] The *meta* value here is again higher than that observed from Friedel–Crafts alkylations in nitromethane (60–61% *ortho*, <2% *meta*, and 38% *para*; *ortho/para* = 1.6).[26] The high *ortho/para* could be a result of "linear coordination"[26] since that cationic species is known to attack ethers.[13] However, since no ether cleavage products were observed, no conclusion can be made from the data.

The large amount of *meta* isomer from the isopropylation of toluene and anisole is probably a result of enhanced reactivity of the cationic species from amine diazotizations. Isomerization and disproportionation[28] are possible; however, they are not expected to be of importance since strong Lewis acids are not present. However, positional rearrangement in the σ complex, prior to proton elimination, may occur and this may account for the higher *meta* content.

Alkylation of arenes *via* aprotic diazotization is consistent with the postulate of cationic intermediates. The minor amounts of rearrangement suggest SN2 displacement of arene on a diazonium ion–gegenion pair, and the similarity of product composition in the alkylarene and acetate fraction implies that the partitioning of the diazonium ion and rearranged carbonium ion toward arene and gegenion is identical. Relative rate studies and isomer composition of the cymenes indicate that an intermediate of enhanced reactivity is involved. This is expected of ions generated in aprotic solvents.

Experimental Section

Reaction Conditions. The procedure developed earlier[29] was employed. A solution of the amine (10 mmol), acid (10 mmol), and decyl nitrite[7] (11 mmol) in 100 ml of arene[30] was heated to reflux. After completion of nitrogen evolution the mixture was directly glpc analyzed. Glpc analyses were carried out on a Wilkens-Varian Hy-Fi (Model 600D) using a $^{1}/_{8}$ in. o.d. 15 ft (15%) Apiezon L (Chromsorb P, 60–80 mesh) column. The yields were determined by gas chromatography using an internal standard.

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(26) P. Kovacic and J. J. Hiller, *J. Org. Chem.*, **30**, 1581 (1965).

(27) We acknowledge with thanks Dr. M. Kurz and Professor P. Kovacic for authentic samples of *o*-, *m*-, and *p*-isopropylanisoles.

(28) A type of disproportionation occurs in nitrosation reactions between nitrosonium ion and isopropylbenzene. However the *m*- and *p*-cymenes were preferentially attacked, and this would give lower amounts of *meta* substitution: G. A. Olah and N. Friedman, *J. Am. Chem. Soc.*, **88**, 5330 (1966).

(29) L. Friedman and J. H. Bayless, *ibid.*, **91**, 1790 (1969).

(30) In relative rate studies, mixtures of toluene and benzene (total volume 100 ml) were employed.